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Health and Environmental Effects Profile for Acephate

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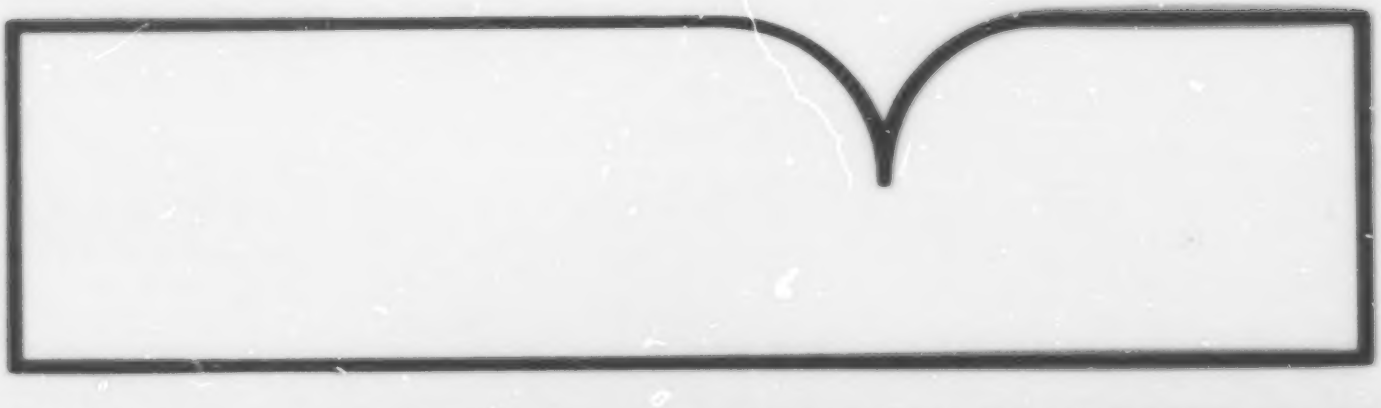

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR ACEPHATE

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for acephate was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Acephate has been evaluated as a carcinogen. The human carcinogen potency factor (q_1^*) for acephate is 6.6×10^{-3} (mg/kg bw/day)$^{-1}$ for oral exposure.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

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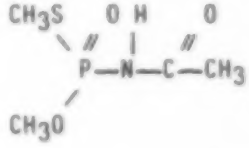
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
bw	Body weight
DNA	Deoxyribonucleic acid
EC_{50}	Median effective concentration
i.p.	Intraperitoneal
LC_{50}	Concentration lethal to 50% of recipients (and all other subscripted dosage levels)
LD_{50}	Dose lethal to 50% of recipients (and all other subscripted dosage levels)
LOAEL	Lowest-observed-adverse-effect level
NOEL	No-observed-effect level
ppm	Parts per million

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Acephate is the common name for O,S-dimethylacetylphosphoramidothioate. Chemical Abstract usage is phosphoramidothioic acid, N-acetyl-, O,S-dimethyl ester. It was introduced in 1971, after field trials in 1969, by the Chevron Chemical Company under the code number "Ortho 12420" and the trademark "Orthene" (BCPC, 1977). Other commercial names for acephate include Acephat (German), Orthene-755, Ortran, Ortril, Acetamidophos and ENT-27822. The structural and molecular formulae for acephate are as follows:



Molecular formula: $C_4H_{10}NO_3PS$

Molecular weight: 183.2

The Chemical Abstract Services (CAS) Registry number is 30560-19-1.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Acephate (as a technical product of 80-90% purity) is a white solid at ordinary temperatures (BCPC, 1977). Selected physical properties are listed below:

Melting point:	82-89°C 72-80°C	(BCPC, 1977) (Ouellette and King, 1977)
Vapor pressure:	1.7×10^{-6} mm Hg at 24°C	(BCPC, 1977)
Water solubility:	6.5×10^{5} ppm 65% at room temperature	(Kenaga, 1980) (BCPC, 1977)
Soil adsorption coefficient, K_{OC}, calculated:	3	(Kenaga, 1980)

BCF, calculated from water solubility:	0.3	(Kenaga, 1980)

At room temperature, acephate is <5% soluble in aromatic solvents and >10% soluble in acetone or ethanol; it is relatively stable and should be stored in a cool place (BCPC, 1977).

1.3. PRODUCTION DATA

Acephate is produced by the acetylation of O,O-dimethylphosphorcamidothioate followed by isomerization (BCPC, 1977). The commercial process uses phosphorous oxychloride as a raw material (SRI, 1976).

The only domestic producer of acephate is Standard Oil of California (Chevron Chemical) in Richmond, CA (SRI, 1983; USITC, 1983). Current production figures are not available, but the plant's capacity to produce acephate is reportedly 1 million lb/year (SRI, 1976).

1.4. USE DATA

Acephate is used as a systemic insecticide (BCPC, 1977). At the recommended foliage rates, its residual activity lasts ~10-15 days. It is effective against a wide range of aphids, thrips, leaf miners, sawflies and lepidopterous larvae, and can be used safely on many crop plants. Formulations include soluble powders, granules and pressurized sprays.

In 1982, 0.5 million acres of tobacco were treated with 0.7 million pounds of acephate (USDA, 1983). In 1979, 0.357 million pounds of acephate were used in treating cotton plants (McDowell et al., 1982). Consumption in 1975 was reportedly 0.5 million pounds, with 0.2 million pounds used in tobacco and 0.3 million pounds used on ornamental plants (SRI, 1976).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

The fate of acephate in water will depend on its ability to undergo chemical, biological and photochemical reactions and partition between the sediments and the atmosphere. The hydrolysis of acephate in water has been studied by Szeto et al. (1979) in the laboratory. Szeto et al. (1979) measured the effect of pH (range 4.0-8.2) on acephate hydrolysis in buffered, distilled water held at 20°C and at 30°C for 20 days; the results are summarized in Table 2-1. For the pH range 4.0-6.9, there is no significant difference in the hydrolysis rate at 20°C compared to 30°C. At pH 6.9, slightly <20% of the initial acephate concentration is hydrolyzed in 20 days. At pH 8.2, hydrolysis is strongly affected by temperature; although 77.9% of the acephate remained at 20°C, only 17.8% remained at 30°C. Szeto et al. (1979) also monitored the amount of methamidaphos (de-acetylated acephate) produced by the acephate hydrolysis and determined that N-de-acetylation is not the primary pathway of non-enzymatic, pH-mediated acephate hydrolysis.

Szeto et al. (1979) have shown that microbial degradation of acephate can be a major mechanism for its disappearance in natural water. Using creek water obtained from British Columbia, Szeto et al. (1979) examined the fate of 1 ppm acephate in the whole water (water plus bottom sediment) and in the water minus the sediment. The water samples were maintained at 9°C for 50 days. Some of the samples were autoclaved to examine the degree of microbial breakdown; the results are summarized in Table 2-2. After 50 days, acephate degradation in non-autoclaved samples was more than twice the degradation in autoclaved samples. This indicates that microbial degradation of acephate in natural waters is significant. Data presented in Section 2.3. indicate that soil microorganisms can biograde acephate.

TABLE 2-1

Hydrolysis of Acephate in Buffered, Distilled Water
Held at 20°C and 30°C for 20 Days*

pH	Percent of Acephate Remaining	Percent of Methamidophos Present
20°C		
4.0	97.8	0.2
5.0	92.7	0.2
5.6	88.2	0.2
6.0	86.1	0.2
6.9	84.2	1.0
8.2	77.9	4.5
30°C		
4.0	95.5	0.5
5.0	90.2	0.2
5.6	83.8	0.2
6.0	83.0	0.2
6.9	82.5	1.7
8.2	17.8	4.3

*Source: Szeto et al., 1979

TABLE 2-2

The Fate of 1 ppm Acephate in Creek Water at 9°C
(Effects of Autoclaving and Bottom Sediments)*

Day	Percentage of Acephate Remaining		
	Water Only	Water Plus Bottom Sediment	
		In Water	In Bottom Sediment
		Not Autoclaved	
7	77.6	37.0	19.1
21	88.0	29.3	14.8
34	58.4	35.5	2.1
50	45.2	25.5	2.3
		Autoclaved	
43	75.7	53.0	10.0
50	76.4	55.0	9.7

*Source: Szeto et al., 1979

Szeto et al. (1979) also demonstrated that acephate degraded more rapidly in water with sediment than in water alone. In addition to the creek water data presented in Table 2-2, similar data, with respect to sediment vs. no sediment, was developed for pond water obtained in British Columbia. In pond water only, ~20% of the acephate degraded in 42 days, while in the pond water plus sediment, ~80% degraded in 42 days. Szeto et al. (1979) noted that microbial breakdown due to the presence of sediment did not account for all of the additional degradation in the samples with sediment. They suggested that interactions between acephate and colloidal sediment particles initiated a hydrolysis mechanism responsible for degradation.

Data specific to the photodecomposition of acephate were not located in the available literature.

The transport of acephate from water due to volatilization has not been examined comprehensively. Szeto et al. (1979) reported that acephate could not be shown to escape into the atmosphere. This is predictable, as acephate is highly soluble in water.

Data from Szeto et al. (1979) also indicate that acephate in the water environment will remain more in solution than partitioned into sediments. This is also reasonable due to the high water solubility of acephate. Twenty percent of the applied acephate was in the bottom sediments after 2 days (pond) and 7 days (creek).

The bioconcentration of acephate has been studied in an aquatic model ecosystem (Sanborn, 1974; Booth, 1975). Acephate did not bioaccumulate in any of the organisms in the ecosystem, including algae, clam, crab, daphnia, elodea, fish, mosquito and snail; no detectable levels of acephate were found in any organism. Geen et al. (1981) and Hussian and Oloffs (1980) introduced acephate into a natural river to simulate the effect of an aerial

spraying program upon fish and insects. The acephate (~1 ppm) was rapidly taken up by the fish and insects; however, the acephate levels were reduced to non-detectable concentrations within 24 hours (detection level not available from reference sources used). Kenaga (1980) has predicted a BCF of 0.3 for acephate based upon its water solubility, which indicates that acephate is unlikely to bioconcentrate.

The persistence of acephate in the aquatic environment has been examined by several investigators. Sanborn (1974), in the previously noted model ecosystem, found that after 35 days <1% of the ^{14}C level in the water was attributable to acephate. Geen et al. (1981) and Hussian and Oloffs (1980) found no detectable levels of acephate in water 4 days after being introduced into a natural river to simulate aerial spraying. Traces (no limits given) of acephate were detected in the river sediment. The persistence of acephate in creek and pond water and sediment taken from British Columbia by Szeto et al. (1979) has already been discussed. From this study, it appears that the persistence of acephate in the aquatic environment is dependent upon several factors, including microbial population, collodial sediments, pH and temperature.

2.2. AIR

Data specific to the fate and transport of acephate in the atmosphere were not located in the available literature. Due to the very high solubility of acephate in water, it is possible that acephate in the gaseous phase may be dissolved into cloud or rain droplets and subsequently removed by rainfall.

2.3. SOIL

The fate and transport of acephate in the soil has not been studied comprehensively; however, from the available data it appears that microbial

degradation and chemical hydrolysis may be the predominant mechanisms by which acephate is lost from soil. Rosenberg and Alexander (1979) found that bacteria enrichment cultures isolated from soil and sewage sources were able to use acephate as a sole source of phosphorus; however, the acephate was unable to be used as a sole carbon source. Additionally, Rosenberg and Alexander (1979) found that cell-free extracts of Pseudomonas were able to catalyze the degradation of acephate. Focht and Joseph (1974) applied acephate to a loamy sand, a silt loam and a clay loam at twenty times the recommended rate of 1 ppm and found that population levels of actinomycetes, bacteria and fungi were not significantly effected over a 50-day interval. In the silt loam soil, the acephate appeared to stimulate respiration to a limited extent. Szeto et al. (1979) determined that microbial degradation of acephate was significant in the aquatic environment (see Section 2.1.), but did not isolate the microorganisms responsible for the degradation.

While chemical hydrolysis of acephate in the soil has not been studied, the hydrolysis data presented in Section 2.1. concerning the water environment may indicate that acephate is susceptible to hydrolysis in moist soils.

Information regarding the transport of acephate in soil from leaching was not located in the available literature. Kenaga (1980) has predicted a soil adsorption coefficient (K_{oc}) of 3 for acephate based upon its water solubility. Compounds having a K_{oc} value <100 are considered moderately to highly mobile. As noted in Section 2.1., Szeto et al. (1979) found that up to 3 weeks after introduction of acephate into natural whole water obtained from a creek and a pond, about one-fifth to one-third of the acephate was partitioned into the sediments, while to remainder was in the water.

The volatilization of acephate from the soil has not been studied; acephate is probably not significantly volatile from soil surfaces due to its low vapor pressure.

Baik et al. (1982) examined the persistence of acephate in rice paddy soil in the laboratory. The half-life of acephate was 3-4 days in aerobic conditions and 13-14 days in flooded conditions. Focht and Joseph (1974) reported that acephate is short-lived (no time given) in soil and is graded primarily through S-demethylation. A small portion (10-15%) is also degraded to the pesticide monitor via deacylation.

3. EXPOSURE

3.1. WATER

The U.S. EPA STORET Data Base reports the analysis of acephate in eight whole water (water plus sediment) samples. The mean concentration of acephate in these whole water samples was reported to be 47 µg/ℓ, with a range of concentration of 0.0-135 µg/ℓ. Other monitoring data for acephate exposure were not located in the available literature. No available data indicate acephate exposure from finished drinking water.

3.2. FOOD

Data specific to acephate exposure in finished foods was not found in the available literature. Baik et al. (1982) detected acephate residues of 0.01-0.53 ppm in unpolished Korean rice on which acephate was used as an insecticide; the time interval between application and analysis was not stated in the available abstract.

3.3. INHALATION

Wright et al. (1981) monitored the ambient air of vacant dormitory rooms at North Carolina State University for insecticide levels following applications of individual insecticides. The ambient air was sampled with personnel type air samplers with Midget Impingers that were placed near the center of the test room. The rooms in the dormitory had a mean volume of 61 m^3 and two windows that remained closed during the test. The insecticide was applied into cracks and crevices and to other sites in the room usually inhabited by cockroaches. The ambient air was monitored before treatment (to ascertain background levels, if any), immediately after treatment, and at 1-, 2- and 3-day intervals. The average amount of acephate applied in the test rooms was 3.2 g active ingredient. Before treatment, acephate was not detectable in the air (detection limit of 0.01 µg). Immediately after

treatment, the airborne concentration of acephate was 1.3 µg/m³. After a 1-day interval, the concentration was 2.9 µg/m³; after 2 days, it was 0.5 µg/m³ and after 3 days, it was 0.3 µg/m³. The reason for the rise in concentration at the 1-day interval was unknown.

3.4. DERMAL

Monitoring data for acephate exposure on the skin of American workers were not located in the available literature.

4. PHARMACOKINETICS

Pertinent data regarding the absorption, distribution and excretion of acephate were not located in the available literature.

Regarding the metabolism of acephate, Ando and Wakamatsu (1982) reported that the anti-cholinesterase effect of acephate decreased after incubation with a 9000 g supernatant mixture derived from liver (animal source not mentioned). This indicated that at least some of the acephate is inactivated in the liver. The FAD-dependent monooxygenase from the pig, however, had no effect on acephate in vitro (Hajjar and Hodgson, 1982). A gradual decrease in blood and liver glutathione was observed by Patel and Chakrabarti (1982) in rats given 60 mg acephate/rat/day orally, which may indicate that glutathione is involved in the metabolism of acephate.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of acephate were not located in the available literature.

5.2. MUTAGENICITY

Assays assessing the genotoxic potential of acephate are summarized in Table 5-1. Acephate has consistently caused reverse mutations in Salmonella typhimurium in the TA100 strain (Moriya et al., 1983; Poole et al., 1977). Negative results have been reported in all other S. typhimurium strains (Poole et al., 1977). Although some Chinese reports indicate acephate is nonmutagenic (Jeang and Li, 1978; Anonymous, 1978), the research is presented in abstracts that contain no information on the strains used or the presence or absence of metabolic activation. The dose-response curve for the mutagenicity of acephate is the same with and without the S-9 mixture (Moriya et al., 1983), which indicates that metabolic activation and/or deactivation is not a major factor in controlling the mutagenicity of acephate.

Hanna and Dyer (1975) reported increased reverse mutations in E. coli strains WP2 and WP2 uvr A after 48 hours and in strain WP12 after 72 hours, in the absence of any metabolic activating system. Poole et al. (1977) also reported that acephate was mutagenic to E. coli strain WP2 in the absence of any metabolic activating system. However, Waters et al. (1982) reported that acephate did not cause any increase in mutations in E. coli WP2 uvr A with or without a metabolic activating system.

In the eukaryotic yeast cells, acephate increased the rate of reverse mutation and mitotic recombination in all the assays reported (Riccio et al., 1981; Waters et al., 1982). Mutagenicity testing in yeast was positive regardless of the presence or absence of S-9 mixture. Griffiths (1979)

TABLE 5-1

Mutagenicity of Acephate

Assay	Indicator Organism	Strain	Concentration or Dose	Application Method	Activation System	Response*	Comments	Reference
Reverse mutation	Salmonella typhimurium	TA1530 TA1535 his C117 his G46	5-10 µg or crystal	spot test/plate incorporation	-	-	It appears that several related were used during the experiment, but acephate did not appear mutagenic in any of them.	Hanna and Dyer, 1975
Reverse mutation	S. typhimurium	TA100 TA98 TA1535 TA1537 TA1538	500-50,000 µg/plate	plate incorporation	+/- +/- +/- +/- +/-	+ - - - -	All the strains were negative except TA100. Metabolic activation with S-9 had no effect on the dose-response curve.	Moriya et al., 1983
Reverse mutation	S. typhimurium	TA1535 TA1537 TA1538 TA98 TA100	≤10 mg/plate	plate incorporation	+/-	+	Responses were not reported individually for each strain or for the presence or absence of S-9.	Poole et al., 1977
Reverse mutation	Escherichia coli	WP2 WP2uvrA CM561 CM571 CM611 WP67 WP12	crystal	spot test	-	+ + - - - - +	Mutagenicity was observed in strains WP2 and WP2uvrA after 48 hours of incubation, and in strain WP12 after 72 hours of incubation. All other strains were negative.	Hanna and Dyer, 1975
Reverse mutation	E. coli	WP2	NR	NR	-	+	Little information was available in this abstract.	Poole et al., 1977
Reverse mutation	E. coli	WP2hcr	≤5000 µg/plate	plate incorporation	+	+	NC	Moriya et al., 1983
Mitotic recombination	Saccharomyces cerevisiae	D3	NR	NR	+	+	Little information was available in this abstract.	Poole et al., 1977
Mitotic recombination	S. cerevisiae	D3 D7	NR	NR	+/-	+	Acephate was mutagenic in both strains of yeast. Data taken from an abstract.	Riccio et al., 1981
Reverse mutation	S. cerevisiae	D7	NR	NR	+/-	+	Responses were not reported individually for the presence or absence of S-9.	Waters et al., 1982

TABLE 5-1 (cont.)

Assay	Indicator Organism	Strain	Concentration or Dose	Application Method	Activation System	Response*	Comments	Reference
Non-disjunction	Neurospora crassa	NR	NR	plate incorporation	NR	-	The significance of negative results was not clear; perhaps the concentration was too low. Repeat tests were not consistent.	Griffiths, 1979
Rec-assay	E. coli	pol A$^+$ pol A$^-$	NR	disk incorporation	NR	-	NC	Waters et al., 1982
Rec-assay	E. coli	NR	NR	NR	NR	-	Little information was available in this abstract.	Simmon, 1979
Recessive lethal	Drosophila melanogaster	NA	NR	NR	NA	-	NC	Waters et al., 1982
Forward mutation	mouse lymphoma cells	L51784	NR	in culture medium	NR	+	NC	Waters et al., 1982
Unscheduled DNA synthesis	WI-38	NA	NR	in culture medium	NR	+	Little information was available in this abstract.	Simmon, 1979
Mouse micronucleus assay	mouse	NR	NR	gavage/ intraperitoneally	NA	-	NC	Waters et al., 1982
Dominant lethal	mouse	NR	NR	in diet	NA	-	NC	Waters et al., 1982
Sister chromosome exchange	hamster cells	NR	NR	in culture medium	NR	+	NC	Waters et al., 1982
Sister chromosome exchange	Muntiacus muntjak	NR	NR	in culture medium	NR	+	Little information was available because the results were reported in an abstract.	He et al., 1982

*Responses: +, positive; -, negative; ±, negative with and without S9 activation system; ±, positive with and negative without S9 activation system; ∓, negative with and positive without S9 activation system

NA = Not applicable; NR = not reported; NC = no comment

reported that acephate did not increase the rate of non-disjunction in Neurospora crassa, but also indicated that negative results were difficult to interpret.

In the higher eukaryotic cultured cells and organisms, the results of acephate mutagenicity testing were mixed. Acephate did not produce recessive lethal mutations in Drosophila melanogaster (Waters et al., 1982) or dominant lethal mutations in mice (Waters, 1982). However, an increased rate of forward mutation was reported in cultivated mouse lymphoma cells (L51784) treated with acephate in vitro (Waters et al., 1982). The Waters et al. (1982) paper reported the results of a battery of mutagenicity tests performed on 65 agricultural chemicals and, therefore, the details of the methodology used in each assay of acephate mutagenicity and the data generated are not presented in the report.

Unscheduled DNA synthesis was reported in cultivated WI-38 human fibroblasts when acephate was added to the culture medium (Simmon, 1979). Increased frequency of sister chromatid exchange was reported in Chinese hamster cells (Waters et al., 1982) and in Muntiacus muntjak, red muntjac diploid cells (He et al., 1982), which were cultivated in the presence of acepahte. The work of He et al. (1982) was presented in an English abstract of the original Chinese paper. However, acephate did not increase the number of polychromatophic erythroblasts that contained cytoplasmic micronuclei, which are indicative of chromosome breakage (Waters et al., 1982).

In summary, based upon the positive gene mutation data in both prokaryotic and eukaryotic systems, acephate is considered to possess mutagenic activity. The positive results in unscheduled DNA synthesis in human cells and sister chromatid exchanges in two rodent cell lines further support this conclusion.

5.3. TERATOGENICITY

The only information available regarding the teratogenicity of acephate was found in an abstract of a Chinese study, which described acephate as non-teratogenic in rats (Huang et al., 1980).

5.4. OTHER REPRODUCTIVE EFFECTS

Haley et al. (1973) exposed three generations of rats, beginning with the F_0 generation at weaning, continuously to acephate at dose levels of 1.5, 5 and 15 mg/kg/day. No effect was reported at the dose level of 1.5 mg/kg/day; however, decreased mating and fertility indices appeared by the F_{2a} generation at dose levels of 5 and 15 mg/kg/day. No other data were available in the review of this unpublished study provided by Clegg (1979).

5.5. SUBCHRONIC AND CHRONIC TOXICITY

Pertinent data regarding the subchronic and chronic toxicity of acephate were not located in the available literature.

5.6. OTHER RELEVANT INFORMATION

Data regarding the acute toxicity (LD_{50}) of acephate are presented in Table 5-2.

Seven impurities found in technical grade acephate were identified and four of them were tested for their potentiating effect on the toxicity (LD_{50}) of purified acetate. Two had no effect, while O,O,S-trimethyl phosphorothioate caused a slight potentiation and O,O-dimethyl N-acetylphosphoramidothioate caused a significant decrease in mouse toxicity. After storage for 6 months at 40°C, the toxicity of acephate to mice was reduced to 66% of the original toxicity. The concentration of methamidophos, however, one of the impurities in acephate that is substantially more toxic to mice than acephate, was found to increase. No explanation of these apparently contradictory findings was proposed by the authors (Umetsu et

TABLE 5-2

Acute Toxicity of Acephate

Species	Route	LD_{50} (mg/kg)	Reference
Rats	oral	males 945[a]; females 861[a]	BCPC, 1977
Rats	oral	females 1800[a]	Umetsu et al., 1977
Rats	oral	females 1480[a]	Umetsu et al., 1977
Mice	oral	361[a]	BCPC, 1977
Mice	oral	females 500[a]	Umetsu et al., 1977
Mice	oral	females 425[a]	Umetsu et al., 1977
Rabbits	dermal	>2000[a]	BCPC, 1977

[a]Technical grade acephate

[b]Purified acephate

al., 1977). Kobayashi (1978) did not find any synergism (endpoint not described in abstract) when acephate was used in combination with other organophosphorous insecticides. Gaughan et al. (1980) reported that acephate was a very weak potentiator of the toxic effects (LD_{50} and liver esterase activity) of fenvalerate and malathion. The two other organophosphorous insecticides were administered by i.p. injection 1 hour after the i.p. administration of acephate.

When rats were injected subcutaneously with acephate (25 mg/100 g bw/day) for 4 weeks and 8 weeks, a decrease in the riboflavin (Deotare and Chakrabarti, 1981a) and thiamine (Deotare and Chakrabarti, 1981b) content in rat tissues was observed. The decrease was more pronounced after 8 weeks for both thiamine and riboflavin. Concomitant with the decrease in thiamine, an increase in pyruvic and lactic acid was observed. In addition, glycogen stores in the liver were greatly reduced and blood glucose was slightly elevated (Deotare and Chakrabarti, 1981b). Concomitant with a decrease in riboflavin, succinic dehydrogenase activity was reduced (Deotare and Chakrabarti, 1981a). Normal levels of pyruvic and lactic acids, succinic dehydrogenase, glycogen and glucose were restored when thiamine (100 mg/100 g bw/day) and riboflavin were given concurrently with acephate (Deotare and Chakrabarti, 1981a,b).

Workers exposed to acephate did not have reduced levels of serum cholinesterase when their serum level of acephate was <200 ppm (Ando and Wakamatsu, 1982). No additional details were reported.

6. AQUATIC TOXICITY

6.1. ACUTE EFFECTS

The toxicity and lethal levels of acephate have been reported for several freshwater and marine species of fish and aquatic invertebrates. Acephate is generally regarded as having a relatively low toxicity to aquatic species. In freshwater fish (Table 6-1), 96-hour LC_{50}'s have not been specifically determined due to low mortalities, even at the highest levels tested (Johnson and Finley, 1980). For the rainbow trout, generally regarded as a sensitive species, the 96-hour LC_{50} value was 1100 mg acephate/. when tested at 10°C (Johnson and Finley, 1980). The 96-hour LC_{50} values in other species reported by these authors were greater than the highest test concentration (usually 1000 mg/ℓ) (Table 6-1).

Water temperature appears to affect the toxicity of acephate to fish. Duangsawasdi and Klaverkamp (1979) reported LC_{50} values for rainbow trout, Salmo gairdneri, to be 3160, 2890 and 1880 mg/ℓ, respectively, following 24-25 hours of exposure at 8, 15 and 22°C. Increased water temperature was proportional to increased acephate toxicity.

Freshwater invertebrates appear more sensitive to acephate than fish; this may be significant, since these crustaceans and insects are often food species of the fish (Table 6-2). Median lethal levels for the amphipod, Gammarus pseudolimnaeus, were reported to be >25 (Woodward and Mauck, 1980) and 50 mg/ℓ (Johnson and Finley, 1980). In species of stonefly, LC_{50} values ranged from 6.4-21.2 mg/ℓ for 96 hours of exposure. Data reported by Woodward and Mauck (1980) suggested that acephate toxicity in stoneflies is related to the acidity of water. The 96-hour LC_{50} values for Pteronarcella bodia were 6.4, 9.5 and 21.2 when tested at 12°C and pH 6.5, 7.5 and 8.5, respectively.

TABLE 6-1

Acute LC_{50} of Acephate to Freshwater Fish

Species	Duration (hours)	Concentration	Method	Reference
Rainbow trout, Salmo gairdneri	24	3160	static, 8°C	Duangsawasdi and Klaverkamp, 1979
	24	2890	static, 15°C	
	25	1880	static, 22°C	
Rainbow trout, S. gairdneri	96	1100	static, 10°C	Johnson and Finley, 1980
Cutthroat trout, Salmo clarki	96	>100	static, 12°C	Johnson and Finley, 1980
Brook trout, Salvelinus fontinalis	96	>100	static, 12°C	Johnson and Finley, 1980
Fathead minnow, Pimephales promelas	96	>1000	static, 20°C	Johnson and Finley, 1980
Channel catfish, Ictalurus punctatus	96	>1000	static, 22°C	Johnson and Finley, 1980
Bluegill sunfish, Lepomis macrochirus	96	>1000	static, 20°C	Johnson and Finley, 1980
Yellow perch, Perca flavescans	96	>50	static, 7°C	Johnson and Finley, 1980
Cutthroat trout, S. clarki	96	>100	static, 12°C	Woodward and Mauck, 1980
Rainbow trout, S. gairdneri	24	895-1050	static	Klaverkamp et al., 1975

TABLE 6-2

Acute LC_{50} of Acephate to Freshwater Invertebrates

Species	Duration (hours)	Concentration	Method	Reference
Amphipod, *Gammarus pseudolimnaeus*	96	>25	static, 12°C	Woodward and Mauck, 1980
Amphipod, *G. pseudolimnaeus*	96	>50	static, 12°C	Johnson and Finley, 1980
Stonefly, *Pteronarcella* sp.	96	9.5	static, 12°C	Johnson and Finley, 1980
Stonefly, *Pteronarcella badia*	96	6.4	static, 12°C,	Woodward and Mauck, 1980
	96	9.5	static, 12°C, pH 7.5	
	96	21.2	static, 12°C, pH 8.5	
Stonefly, *Skwala* sp.	96	12.0	static, 7°C	Johnson and Finley, 1980
Midge, *Chironomus* sp.	96	>1000	static, 20°C	Johnson and Finley, 1980

The lethal effects of acephate on marine species of fish and invertebrates were determined in tests conducted by the Environmental Research Laboratory (1981) (Table 6-3). The 96-hour LC_{50} determined for sheepshead minnows, Cyprinodon variegatus, during static testing was 3200 mg/ℓ. In spot, Leiostomus xanthurus, exposed at 100 mg acephate/ℓ in static conditions for 96 hours, mortality was 23%. The 96-hour LC_{50} for pinfish, Lagodon rhomboides, exposed in a flow-through system was 85 mg acephate/ℓ.

No mortality was noted in pink shrimp, Penaeus duorarum, exposed at 10 mg acephate/ℓ for 96 hours at 25°C in static conditions. In flow-through tests conducted at 22°C, mortality among the shrimp was noted and the 96-hour LC_{50} value was determined to be 3.8 mg/ℓ. Similarly, the 96-hour LC_{50} for mysid shrimp in flow-through tests at 22°C was 7.3 mg acephate/ℓ. The 48-hour EC_{50} for abnormal development in embryos of the Eastern oyster in static tests (25°C) was 150 mg/ℓ.

The toxic effects of acephate on rainbow trout, S. gairdneri, included increased heart and ventilatory rates and gasping (Duangsawasdi and Klaverkamp, 1979). Cholinesterase activity of gill, heart, serum and erythrocytes was notably inhibited within 3 hours of exposure, while inhibition of skeletal muscle and brain chlorinesterase was delayed. This study suggests that the cardiovascular system and gills are important sites of the toxic effects of acephate.

6.2. CHRONIC EFFECTS

Mysid shrimp, Mysidopsis bahia, were exposed to acephate at 0.52, 0.58, 1.4, 2.0 and 4.2 mg/ℓ for up to 28 days (Environmental Research Laboratory, 1981). During the exposure period, shrimp matured and produced brood pouches. At 4.2 mg acephate/ℓ, shrimp began to die on day 7, while deaths occurred after 14 days in groups exposed at 1.4 and 2.0 mg/ℓ. At 0.58 mg

TABLE 6-3

Acute Lethal Effects of Acephate to Marine Species*

Species	Duration (hours)	Concentration	Method	Effect
Sheepshead minnow, Cyprinodon variegatus	96	3200	static, 25°C	10% mortality
Spot, Leiostamus xanthurus	48	100	static, 25°C	10% mortality
	72	100	static, 25°C	17% mortality
	96	100	static, 25°C	23% mortality
Pinfish, Lagodon rhomboides	48	120	flow-through; 22°C	50% mortality
	72	120	flow-through; 22°C	85% mortality
	96	120	flow-through; 22°C	95% mortality
	96	85	flow-through; 22°C	LC_{50}
Pink shrimp, Penaeus duorarum	96	10	static; 25°C	No mortality
	96	3.8	flow-through; 22°C	LC_{50}
Mysid shrimp, Mysidopsis bahia	96	7.3	flow-through; 22°C	LC_{50}
Eastern oyster, Crassostrea virginica	48	150	static; 25°C	EC_{50}; mortality and abnormal development

*Source: Environmental Research Laboratory, 1981

acephate/ℓ, mortality was not different from controls at the end of the study period. The time to brood pouch formation appeared to be retarded in shrimp exposed at levels >2.0 mg acephate/ℓ. The average number of offspring per brood was significantly reduced in shrimp exposed at 2.0 and 4.2 mg/ℓ compared to controls (4.9 and 3.4 offspring vs. 8.4 in controls). The maximum acceptable toxicant concentration for this species was, therefore, reported to be between 0.58 and 1.4 mg acephate (Environmental Research Laboratory, 1981).

6.3. PLANT EFFECTS

The effect of acephate on the growth of the marine diatom, Skeletonema costatum, was examined in static tests conducted for 4 days (Environmental Research Laboratory, 1981). Concentrations of acephate tested were 0.1, 1.0, 5.0, 10.0 and 50.0 mg/ℓ and growth was determined by optical density of 525 nm. None of the acephate concentrations tested caused a decrement in absorbance of algal cultures. The EC_{50} for growth inhibition of this alga was, therefore, >50 mg acephate/ℓ.

6.4. RESIDUE

In laboratory and field testing, Lyons et al. (1976) concluded that the high water solubility of acephate contributed to its low accumulation in tadpoles. Residual levels of acephate in tadpoles were usually very near levels found in the ambient water. Geen et al. (1981) exposed yearling rainbow trout to acephate in a natural stream situation and examined the uptake and persistence of residues in these fish and aquatic insects and sediments. Acephate was rapidly taken up by fish and insects and adsorbed to sediments. Methamidophos was regarded as a more toxic residue and was found in fish and insects. Residue levels decreased rapidly to trace levels by 24 hours and were not detected by 96 hours post-treatment. In studies

conducted in the field during acephate spraying, Rabeni and Stanley (1979) reported that residues remained detectable in the stream for at least 2 days.

6.5. OTHER RELEVANT INFORMATION

Rabeni and Stanley (1979) reported that the feeding habits of fish changed after acephate was sprayed in the area. The number of prey items increased and more terrestrial forms of insects were consumed. The change in diet was related to the increased availability of terrestrial insects; it was not a behavior change due to acephate levels in the water. This study does, however, show the potential for increased consumption of acephate-contaminated insects by fish. The ingestion of contaminated food items did not produce any notable toxic effects on fish.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The U.S. EPA established a tolerance of 0.02 ppm for "acephate and its metabolite methamidophos in or on all food items except those covered by a higher tolerance from use on growing crops" (Federal Register, 1980). A range of tolerances from 0.2 ppm (Federal Register, 1983) for peanuts to 10 ppm (Federal Register, 1975) for celery was established by the U.S. EPA for raw agricultural commodities consumed by humans. The Swiss residue tolerance for acephate is 1.5-2.5 ppm (Seiler, 1977). In 1980, the Chinese estimated the daily allowable ingestion rate of acephate to be 0.018 mg/kg for humans (Huang et al., 1980).

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of acephate were not located in the available literature.

8. RISK ASSESSMENT

No information was available regarding the carcinogenicity and subchronic and chronic toxicity of acephate. Although acephate is described as nonteratogenic in rats, no additional information with which to assess that statement is provided in the abstract of a Chinese study (Huang et al., 1980).

In summary, based upon the positive gene mutation data in both prokaryotic and eukaryotic systems, acephate is considered to possess mutagenic activity. The positive results in unscheduled DNA synthesis in human cells and sister chromatid exchanges in two rodent cell lines further support this conclusion.

Although Ando and Wakamatsu (1982) claim that a serum acephate level <200 ppm is a NOEL, they contend that the activity of serum cholinesterase is not an accurate indicator of acephate exposure, especially at low doses. The Chinese have established the daily allowable ingestion rate of acephate for humans to be 0.018 mg/kg (Huang et al., 1980), but these abstracts contain insufficient information to be useful in deriving an ADI. The only other data available regarding extended exposure of laboratory animals to acephate is the unpublished three-generation study by Haley et al. (1979). Decreased mating and fertility indices beginning with the F_{2a} generation indicated a LOAEL of 5 mg/kg/day for rats. At the next lower dose, 1.5 mg/kg/day, no effects were observed. Although a NOEL is defined by this study, the details of results and experimental design provided in the only available review (Clegg, 1979) of these unpublished data were inadequate for assessment and derivation of an ADI.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment, however, can be presented in this chapter.

The CBI Appendix to this document reviews other animal studies that indicate that acephate is carcinogenic to rats and mice. The weight of evidence from carcinogenicity studies in rats and mice indicates that acephate should be considered to have sufficient animal evidence, and hence be assigned to Group B2 of the proposed EPA ranking scheme for carcinogenic evidence. Using the IARC ranking scheme, the ranking should be Group 2B. Both rankings mean that the substance is probably carcinogenic to humans. A q_1^* for humans of 6.59×10^{-3} $(mg/kg/day)^{-1}$ was calculated from dose-response data for hepatocellular carcinoma in female mice fed acephate in the diet. The calculation of the q_1^* value was made using the linearized multistage model developed by Kenneth Crump and adopted by the U.S. EPA (Federal Register, 1980b). The conversion factor used in the calculation of this q_1^* value for humans (assuming 70 kg body weight) from animal data is the cube root of the body weight ratio (Federal Register, 1980b).

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

These searches were conducted in November, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7th), and the following secondary sources were reviewed:

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